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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/043,665	10/05/1998	STEPHEN JAMES RUSSELL	MEWB112010	7083

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	26

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/043,665	RUSSELL ET AL.	
	Examiner	Art Unit	
	Ram Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 and 11-21 is/are pending in the application.

4a) Of the above claim(s) 13-21 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8,11,12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Amendments and response filed 1-8-02 has been entered.

2. Amendments to claims 1, 5, 7, and 11 have been entered.

3. Claims 13-21 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 10, filed 11-15-99.

4. This application contains claims 13-21 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

5. Claims 1-8, 11 and 12 are under instant consideration.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-8, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method of transforming a population of quiescent hematopoietic stem cells with a nucleic acid encoding a polypeptide for treating a disease or disorder, the method comprising: exposing the quiescent hematopoietic stem cells to a retroviral packaging cell wherein the packaging cell produces a retroviral particle comprising a nucleic acid encoding the polynucleotide for treating a disease or disorder and wherein the packaging cell expresses a nucleic acid encoding a growth factor so that the growth factor is displayed on the surface of the packaging cell and wherein the growth factor displayed on the surface of the packaging cells induces quiescent

hematopoietic stem cells to divide, and the quiescent hematopoietic stem cells are infected by the retroviral particle so that the nucleic acid encoding the polypeptide for treatment is incorporated into the genome of the quiescent hematopoietic stem cells, does not reasonably provide enablement for the claimed method wherein the hematopoietic stem cells are exposed to the retroviral packaging cells in vivo or a method wherein any and all quiescent cells are exposed to retroviral packaging cells in vivo or in vitro, for reasons of record set forth in the previous office action of 6-18-01 and as discussed below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to making and practicing the invention commensurate in scope with these claims.

Additionally, while the specification enables claims 11 and 12 for a method of delivering transformed hematopoietic stem cells to a patient wherein the method comprises the steps of: transforming a population of autologous quiescent hematopoietic stem cells in vitro with a nucleic acid encoding a polypeptide for treating a disease or disorder, the method comprising: exposing the quiescent hematopoietic stem cells to a retroviral packaging cell wherein the packaging cell produces a retroviral particle comprising a nucleic acid encoding the polynucleotide for treating a disease or disorder and wherein the packaging cell expresses a nucleic acid encoding a growth factor so that the growth factor is displayed on the surface of the packaging cell and wherein the growth factor displayed on the surface of the packaging cells induces quiescent hematopoietic stem cells to divide, and the quiescent hematopoietic stem cells are infected by the retroviral particle so that the nucleic acid encoding the polypeptide for treatment is incorporated into the genome of the quiescent hematopoietic stem cells, the specification does not reasonably provide enablement for practicing the claimed method wherein any and all quiescent cells are transformed by the method.

It is noted that claim 1 has been amended to recite "a population of quiescent cells in vitro"; accordingly the rejections pertaining to in vivo method are withdrawn. However, rejection pertaining to: transformation of any and all quiescent cells that can be used in ex vivo treatment method is maintained because such cells could encompass allogeneic, xenogeneic as well as autologous cells. The

specification in examples 1-4 (pages 14-25) discloses method of making retroviral vectors, retrovirus producer cells, packaging cells, infection of cells (progenitor cells from umbilical cord blood and hematopoietic stem cells), characterization of such cells and the proteins produced by these cells by immunoblotting and targeting of cells using said vectors. However, the specification fails to provide any guidance, working example or evidence as to whether the method can be used for transforming any and all quiescent cells, such as senescent cells or non-hematopoietic quiescent cells, or whether the claimed method can be used for transforming quiescent cells in vivo, as discussed below.

The specification on page 5, lines defines quiescent cells as cells that are unlikely to enter mitosis within the next 24 hours in the absence of appropriate growth stimulus and could include stem cells of hematopoietic as well as non-hematopoietic tissues, resting T and B cells, germ cells etc. However, from the teachings of the specification it is not clear whether the method can be used for transforming any and all quiescent cells, such as senescent cells because the requirement of growth factors for different cell types is different and some cells may require more than one growth factors for entering into a new cycle of mitosis. In case of senescent cells, it is not clear whether senescent cells can always be activated to start dividing. For example, Phillips et al (Journal of Cellular Physiology 151:206-212, 1992) disclosed that senescent cells selected with BrdU could not respond to growth factor stimulation of c-fos to start mitosis again. Likewise these authors noted that senescent cells that had already completed their 100% of their proliferative life span could also not be induced with c-fos to go into mitosis. Therefore, at the time of the invention, it was unpredictable whether any and all quiescent cells, for example, senescent cells could be induced to undergo cell division by a growth factor. The specification does not provide any guidance as to how an artisan of skill would have activated cells that were not responsive to a growth factor or how to activate cells that have completed their proliferative life scan.

In addition to senescent cells, different cells may require a combination of growth factors for activation to enter mitosis again. For example, Maurice et al

(Blood 94:401-410, 1999; an article in which the inventor is a co-author), four years after the priority date of the claimed invention noted that display of IL-2 on vector particles might not be sufficient to give highly efficient transduction of primary T cells because such cells would need preactivation by another antigen. Likewise, in airway epithelial cells need prestimulation with keratinocyte growth factor (see discussion on page 408, column 1). Additionally, Maurice et al noted that several aspects of their study pointed to the need for improvements to optimize the strategy for clinical gene transfer (see last paragraph in column 1 on page 408). For example, IL-2 displayed on retroviral particles did not activate the IL-2 dependent cells, rather the activation occurred due to IL-2-SU envelope shed form the vector particles. While the claimed method does not recite using vector particles displaying growth factor, such a condition of shedding growth factor in the culture medium would occur more. This also represents an unpredictability of the claimed method, as to whether the method can be practiced with any and all cells. The specification does not provide any guidance as to how an artisan of skill have activated any and all quiescent cells by the claimed method in light of the unpredictability issues discussed above.

The specification fails to teach what would be the consequence of administering retroviral packaging cells to a mammal or a patient. The specification does not teach whether cells were to be administered by systemic methods or locally to a certain tissue. In any case, such an administration would have resulted in contacting all the cells of the particular tissue or of the entire mammal or patient and if transfer of the retroviral vector was incorporated in cells of the host, there would be indiscriminated expression of the recombinant protein in every cell type and every tissue, if retroviral vector was expressed and the specification does not teach what will be the consequence of such indiscriminated expression of a protein. Alternatively, if the packaging cells were administered to a certain tissue, it would result in infection of all the cell types of the tissue, and again the specification does not teach what would be the consequence of the method. Claimed methods as instantly recited would also encompass a retroviral packaging cell line carrying any and all vector, however, the specification is only enabling for a packaging cell,

which carries a retroviral vector. For example, while a retroviral packaging cell would produce retroviral particles that would infect the target cell, how would a plasmid or another vector be produced by the packaging cell? It is noted that neither the specification nor the prior art, at the time of the invention, taught that a retroviral packaging cell line that carries a plasmid or any vector other than retroviral vector comprising a therapeutic gene would be able to transduce a target cell with the vector.

Regarding the method of treatment, it is noted that the limitation of the method pertaining to transforming any and all quiescent cells would be the same as discussed above. In addition to these limitations there will be the limitation of the immunological tolerance due to the allogeneic or xenogeneic cells. It is well known in the art that one major problem of cell transplantation is rejection of the transplanted cells by the host (see first two paragraphs on page 54 of Kohn DB. Clin. Exp. Immunol. 107:54-57, 1997). As Kohn et al noted even when bone marrow from HLA-identical sibling is used, there is 25-35% chance of mild to moderate graft-versus-host disease from donor derived T lymphocytes responding to recipient antigens. Therefore, the specification fails to teach how can xenogeneic or allogeneic cells could be used. Since, claims do not recite whether the cells being used for administration and transplantation are xenogeneic, allogeneic or autologous, while autologous cells may be more predictable to use for treatment, the immunological implications of the administration of said cells or what would have been the rejection rate in the patients could not be predicted. Furthermore, the method will be complicated by the effect of the growth factor or other protein to be produced in the cell because the growth factor may result in activation of the T cells of the patient resulting in a more severe graft-versus-host disease. The specification does not provide any guidance as to how an artisan would have addressed the issue of rejection of the cells when xenogeneic or allogeneic cells were used in treatment.

Accordingly, limitation of the scope of the claimed invention to an in vitro method of transforming a population of quiescent hematopoietic stem cells with a nucleic acid encoding a polypeptide for treating a disease or disorder, the method

comprising: exposing the quiescent hematopoietic stem cells to a retroviral packaging cell wherein the packaging cell produces a retroviral particle comprising a nucleic acid encoding the polynucleotide for treating a disease or disorder and wherein the packaging cell expresses a nucleic acid encoding a growth factor so that the growth factor is displayed on the surface of the packaging cell and wherein the growth factor displayed on the surface of the packaging cells induces quiescent hematopoietic stem cells to divide, and the quiescent hematopoietic stem cells are infected by the retroviral particle so that the nucleic acid encoding the polypeptide for treatment is incorporated into the genome of the quiescent hematopoietic stem cells, is proper.

Response to Arguments

Applicant's arguments filed 6-18-01 have been fully considered but they are not persuasive. Applicants have argued that the claimed method does not encompass the transformation of senescent cells, however, these arguments are not persuasive because the claim does not exclude senescent cells. Therefore, the claimed invention as recited would encompass senescent cells. Next, regarding the issue of multiple growth factors displayed on the particle, applicants have argued that the specification support that multiple factors could be displayed and that the claimed invention (claim 12) covers such particles. Applicants have argued that the method could be used for transforming allogeneic or xenogeneic cells, however, the issue is: as to how to use these cells for the intended utility i.e. ex vivo therapy. Applicants have used a case (Ex parte Mark), however this case law is not applicable here since the issue in the instant application is of a method of treatment that is known to be unpredictable whereas in the cited case the issue was method of making a protein and the two arts are not comparable since the issues are unrelated. Next applicants argue that presence of inoperative embodiments within the scope does not necessarily render a claim nonenabled. However, applicants are referred to another section of MPEP which states:

"However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work."

As has been discussed above and in the previous office action, the art of ex vivo treatment using xenogeneic and allogeneic cells is unpredictable and therefore, enablement of one species (autologous cells) is not sufficient to support for other species. As has been noted in the previous office actions, neither the specification nor the prior art provides sufficient guidance for practicing the claimed invention in the context of treating a patient with xenogeneic cell transplantation.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4 and 11-12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Luskey et al (Blood 80:3960402, 1992) for reasons of record set forth in the previous office action 6-18-01.

Response to Arguments

Applicant's arguments filed 1-8-01 have been fully considered but they are not persuasive. Applicants' argument that the packaging cell of Luskey et al does not express a recombinant nucleic acid encoding growth factor is not persuasive

because instantly presented claim recites "a retroviral packaging cell line expressing nucleic acid encoding a growth factor" which would read anticipated by the producer cells of Luskey et al. The level of SCF produced in immaterial because there is no such limitation in the claim. Regarding expression on the surface, stromal cells express both membrane bound and secreted, which indicates that the SCF is on the surface of the cells. Accordingly, the rejection in view of Luskey et al is maintained.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 5-8, and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luskey et al (Blood 80:3960402, 1992) in view of Paul et al (US 5,736,387, 4-7-1998, effective filing date 6-1-94) for reason of record set forth in the previous office action of 6-18-01 and as discussed below.

It is noted that applicants have amended claims 11 and 12 wherein the packaging cells express recombinant growth factor.

As noted in the previous office action, Luskey et al teach that prestimulation of bone marrow with various cytokines including stem cell factor increases the retroviral-mediated gene transfer (human ADA encoding cDNA) into murine hematopoietic stem cells (HSC) (see the abstract and also materials and methods section). Bone marrow cells were stimulated with growth factors and prestimulated cells were cocultured with producer cells. Afterwards, non-adherent cells from the coculture were injected into syngeneic recipient mice. Luskey et al also teach that transformed cells when administered to mice show expression of hADA into the peripheral blood and that prestimulation with cytokines and growth factors results into higher levels of hADA expression in mice (see last paragraph in column 2 on

page 398 continued on page 399, column 1). Luskey et al further discusses that the hematopoietic microenvironment may play an important role in the maintenance of reconstituting HSC. Additionally, they note that there is a significant role for the presentation of steel factor or stem cell factor in the context of the microenvironment and that stromal cells (producer cells) express both membrane-bound and secreted SCF, although the level or protein expression is low (see first full paragraph in column 2 on page 401). They conclude that use of the recombinant SCF during prestimulation of the target HSC improves gene transfer efficiency into a primitive stem cell population and may be useful in the further application of gene transfer methods into the HSC of larger animal species, where the efficiency of gene transfer into long-lived stem cells is still problematic (last sentence in the last paragraph in column 2 on page 401). Luskey et al does not teach a fusion protein of the growth factor with a viral envelope protein wherein the growth factor is attached to the N-terminus of the retroviral envelope protein.

Paul et al teaches envelope fusion vectors that can be used in gene delivery. The vectors comprise chimeric targeting proteins that specifically alter the host range of the vector and the chimeric or fusion protein contains a ligand moiety that binds to receptors present on target cells and an uptake moiety that is capable of promoting the entry of the vector into the target cell. The ligand moiety is a cytokine that acts upon target cells and the uptake moiety is derived from a retroviral envelope protein (see abstract). Paul et al teach a vectors wherein IL-2 encoding sequences are fused at the N-terminal of envelope sequences of amphotropic murine retrovirus or of ecotropic murine virus (see figures 2 and 4 and examples 1 and 6). They also teach packaging cells that are transfected with said vector and retroviral particles produced by these cells (see examples 2,3 and 6, also see claims). Paul et al also teaches that the fusion protein of their invention can be used to modulate the targeted cells in accordance with the activity of the cognate cytokine (cytokine fusion partner of the growth factor-envelope fusion protein). They further assert that fusion protein will provide a combination of activities, such as, binding to specific target cells, delivery of the vector nucleic acid into the cell and cytokine modulation of the cells targeted. Such activities will be

advantageous for in vivo gene delivery where it may be otherwise problematic or impossible to induce the targeted cells to divide and thus promote stable incorporation of the transferred gene (see lines 8-32 in column 15). Paul et al further assert that ligand moieties derived from flk2 ligand, that is specifically expressed on early hematopoietic cells or stem cells, can also be expressed as fusion protein of their invention and such a fusion protein could be used to direct infection to lymphohematopoietic progenitor cells (see lines 56-67 of column 15 continued in lines 1-7 of column 6).

Accordingly, at the time of the invention, it would have been obvious to one of ordinary skill in the art to transform the producer cells of Luskey et al with the envelope fusion vector of Paul et al so that the producer cells express the envelope growth factor because it would have allowed an increased number of the growth factor on the membrane of the producer cells, which in turn would have facilitated the efficiency of the infection of HSC by the retroviral vector produced by the producer cells and then use these producer cells to transform hematopoietic stem cells, and use the hematopoietic cells in treatment of diseases, such as ADA deficiency (see the last paragraph in column 2 on page 401). An artisan would have been motivated to express the fusion protein on the membrane of the producer cells because the producer cells have low concentration of the endogenous growth factor such as the steel cell factor and because presentation of the stem cell factor on the membrane would have provided a better presentation of the stem cell factor in context of the producer cell microenvironment and hematopoiesis and also because the fusion protein will provide a combination of activities, such as, binding to specific target cells, delivery of the vector nucleic acid into the cell and cytokine modulation of the cells targeted (see the first full paragraph in column 2 on page 401). Such activities will be advantageous for in vivo gene delivery where it may be otherwise problematic or impossible to induce the targeted cells to divide and thus promote stable incorporation of the transferred gene (see lines 8-32 in column 15 in Paul et al). Furthermore, this would have eliminated the step of prestimulation of the HSC with the steel factor and cytokines before coculture with the producer cells.

Regarding claim 6, it is noted that fusion protein constructs with a cleavable linker between two polypeptides were known in the prior art for other purposes. But the presence of absence of the cleavable linker is not relevant for the use of the instantly claimed method.

Response to Arguments

Applicant's arguments filed 1-8-01 have been fully considered but they are not persuasive. Applicants argue that Paul et al does not teach a situation where the vector to be transduced does not encode a recombinant growth factor, however, these arguments are not persuasive because the instantly claimed invention does not recite any such limitation. Applicants do not provide any evidence as to why the growth factor in case of Paul et al would not be expressed on the surface of the producer cells, in fact it was displayed on the surface the envelop of the fusion protein would not function as intended. It is reiterated that claim 1 does not limit that the growth factor displayed on the surface of the packaging cell and the polypeptide for treating a disease are expressed from two separate vectors or one vector. Accordingly, applicant's arguments are moot.

12. Claim 3 rejected under 35 U.S.C. 103(a) as being unpatentable over Luskey et al (Blood 80:3960402, 1992) and Paul et al (US 5,736,387, 4-7-1998, effective filing date 6-1-94) as applied to claims 1,2, 4-5, and 7- 8 above, and further in view of Lyman et al (US 5,554,512, 9-10-1996, effective filing date 5-24-93), for reasons of record set forth in the previous office action of 6-18-01.

Response to Arguments

Applicant's arguments filed 1-8-01 have been fully considered but they are not persuasive. Applicants have argued that Lyman et al does not remedy the deficiencies of Luskey et al or Paul et al and that it teaches soluble ligand rather than membrane bound and therefore teaches away from the instant invention. However, these arguments are not persuasive because Lyman et al provides the

cDNA for flt3 ligand, teaches that it regulates growth and differentiation of stem cells and progenitor cells (lines 61-67 in column 1), it can be used in stem cell or progenitor cell transplantation (lines 45-52 in column 3), stem cells for transplantation and gene therapy can be grown in flt3 containing culture media (see lines 46-58 in column 7) and that it can be used as fusion protein (lines 50-67 in column 9). Therefore, Paul et al does not teach away from the instantly claimed invention. As noted in the paragraph 11, claim 1 does not limit that the growth factor displayed on the surface of the packaging cell and the polypeptide for treating a disease are expressed from two separate vectors or one vector. Therefore, the question of Lyman remedy this aspect does not arise. As noted in the previous office action, at the time of the invention, An artisan would have been motivated to express the fusion protein on the membrane of the producer cells because the higher expression of growth factors such as the flt3 would have provided a better presentation of the growth factor in context of the producer cell microenvironment and hematopoiesis.

13. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER